

Publication status: This preprint has not been published elsewhere.

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Aldana Belén Recce, Vitória Chesini Malvessi, Vinicius Nomi Hirata, Francisca Bonfada Lang, Gustavo Iansen Garcia, Alexandre Mazzanti, Alexandre Krause, Diego Vilibaldo Beckmann

<https://doi.org/10.1590/0103-8478cr20260152>

Submitted on: 2026-10-21

Posted on: 2026-10-21 (version 1)

(YYYY-MM-DD)



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Aldana Belén Recce¹ (<https://orcid.org/0009-0007-6484-6629>)
Vitória Chesini Malvessi¹ (<https://orcid.org/0009-0005-0596-337X>)
Vinicius Nomi Hirata² (<https://orcid.org/0000-0002-4314-072X>)
Francisca Bonfada Lang² (<https://orcid.org/0009-0007-3717-0758>)
Gustavo Iansen Garcia³ (<https://orcid.org/0009-0008-2832-9242>)
Alexandre Mazzanti^{1,4} (<https://orcid.org/0000-0002-1330-2142>)
Alexandre Krause^{2,5} (<https://orcid.org/0000-0001-8527-6601>)
Diego Vilibaldo Beckmann^{1*,4} (<https://orcid.org/0000-0002-7778-2034>)

¹Programa de Pós-graduação em Medicina Veterinária, Serviço de Neurologia e Neurocirurgia Veterinária, Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), 97105-900, Santa Maria, RS, Brasil. E-mail: beckmann.diego@ufsm.br. *Corresponding author.

²Laboratório Clínico Veterinário, Programa de Pós-graduação em Medicina Veterinária, Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Santa Maria, RS, Brasil.

³Faculdade de Medicina Veterinária, Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Santa Maria, RS, Brasil.

⁴Departamento de Clínica de Pequenos Animais, Serviço de Neurologia e Neurocirurgia Veterinária, Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Santa Maria, RS, Brasil.

⁵Departamento de Clínica de Pequenos Animais, Laboratório Clínico Veterinário, Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Santa Maria, RS, Brasil.

Análise retrospectiva dos achados do líquido cefalorraquidiano segundo a classificação etiológica de doenças neurológicas em cães



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Aldana Belén Recce¹  Vitória Chesini Malvessi¹  Vinicius Nomi Hirata² 
Francisca Bonfada Lang²  Gustavo Iansen Garcia³  Alexandre Mazzanti^{1,4} 
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¹Programa de Pós-graduação em Medicina Veterinária, Serviço de Neurologia e Neurocirurgia Veterinária, Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), 97105-900, Santa Maria, RS, Brasil. E-mail: beckmann.diego@ufsm.br. *Corresponding author.

²Laboratório Clínico Veterinário, Programa de Pós-graduação em Medicina Veterinária, Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Santa Maria, RS, Brasil.

³Faculdade de Medicina Veterinária, Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Santa Maria, RS, Brasil.

⁴Departamento de Clínica de Pequenos Animais, Serviço de Neurologia e Neurocirurgia Veterinária, Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Santa Maria, RS, Brasil.

⁵Departamento de Clínica de Pequenos Animais, Laboratório Clínico Veterinário, Centro de Ciências Rurais (CCR), Universidade Federal de Santa Maria (UFSM), Santa Maria, RS, Brasil.

ABSTRACT: This study characterized the neurological diseases in dogs based on the physical, chemical, and cytological findings of cerebrospinal fluid (CSF). A total of 87 dogs with a final clinical diagnosis of central nervous system disease were included and classified into etiological groups according to the VITAMIN-D mnemonic. The inflammatory, infectious, neoplastic, and degenerative groups were the most prevalent and were included in the statistical analyses, resulting in a total of 101 CSF samples from 75 dogs. The study demonstrated significant associations between age, color, glucose concentration, percentage of polymorphonuclear cells, pleocytosis, and specific etiological groups. The inflammatory group was characterized by dogs with lower body weight and CSF samples with relatively lower glucose levels. The infectious group was characterized by younger dogs, predominantly colorless CSF samples, and marked pleocytosis. The neoplastic group was characterized by older dogs and predominantly colorless CSF samples. The degenerative group was characterized by dogs of intermediate age and body weight, predominantly pigmented CSF samples, and absence of pleocytosis. These findings help refine the interpretation of cerebrospinal fluid analysis, provide epidemiological data from a Brazilian referral hospital population, and reinforce the diagnostic value of CSF analysis in naturally occurring neurological diseases.

Key words: laboratory analysis, neurological diagnosis, veterinary neurology, multivariate models, VITAMIN-D.

Análise retrospectiva dos achados do líquido cefalorraquidiano segundo a classificação etiológica de doenças neurológicas em cães

RESUMO: Este estudo teve como objetivo caracterizar doenças neurológicas em cães com base nos resultados físicos, químicos e citológicos do líquido cerebrospinal (LCS). Para realizar o objetivo, foram incluídos 87 cães com diagnóstico clínico final de doença do sistema nervoso central, distribuídos em grupos etiológicos, conforme a mnemônica VITAMIN-D. O estudo também demonstrou associação significativa entre idade, coloração, glicose, percentagem de células polimorfonucleares, pleocitose e determinados grupos etiológicos. Além disso, os grupos inflamatório, infeccioso, neoplásico e degenerativo foram os mais representativos, sendo analisados os resultados de 101 amostras de LCS de 75 cães. O grupo inflamatório caracterizou-se por cães com menor peso corporal e amostras de LCS com glicose relativamente menor. Enquanto isso, o grupo infeccioso esteve associado a cães mais jovens, amostras predominantemente incolores e marcada pleocitose. Por outro lado, o grupo neoplásico caracterizou-se por cães mais idosos e amostras predominantemente incolores. Por fim, o grupo degenerativo esteve associado a cães com peso e idade intermediários, amostras predominantemente pigmentadas e ausência de pleocitose. Os resultados deste estudo contribuem para o refinamento da interpretação do LCS e reforçam seu valor como ferramenta diagnóstica na prática neurológica veterinária.

Palavras-chave: análise laboratorial, diagnóstico neurológico, neurologia veterinária, modelos multivariados, VITAMIN-D.

1 INTRODUCTION

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space through active secretion and passive
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INTRODUCTION

Cerebrospinal fluid (CSF) is produced in the choroid plexuses of the ventricular system and in the leptomeningeal capillaries of the subarachnoid space through active secretion and passive ultrafiltration of blood plasma (CZARNIAK et al., 2023; RASKIN & MEYER, 2016), and is absorbed into the dural venous sinuses via the arachnoid villi (CHO et al., 2021; SUÑOL et al., 2021). Its main functions include the distribution of nutrients, hormones, and metabolites, waste removal, physical support of the neuroparenchyma, protection against mechanical impacts, and regulation of intracranial pressure (CHO et al., 2021; DE LAHUNTA et al., 2021; DI TERLIZZI & PLATT, 2006).

CSF collection is indicated in dogs presenting neurological signs consistent with encephalopathies, myelopathies, and selected radiculopathies (DEWEY & DA COSTA, 2016; SUÑOL et al., 2021), and is performed by aseptic puncture of the subarachnoid space at the cerebellomedullary cistern (CM) or the caudal lumbar region (CL) (DEWEY & DA COSTA, 2016; DI TERLIZZI & PLATT, 2009). CSF is typically colorless and clear, with a specific gravity of 1.004–1.006, a total nucleated cell count (TNCC) of fewer than 5 cells/ μ L in dogs, absence of erythrocytes, glucose concentration corresponding to 60–80% of blood glucose levels, and low total protein (TP) concentration, ≤ 30 mg/dL in samples from the CM and ≤ 45 mg/dL from the CL (DI TERLIZZI & PLATT, 2006; LAPSINA et al., 2024; RASKIN & MEYER, 2016).

CSF analysis is a diagnostic tool with high sensitivity but low specificity (NGHIEM & SCHATZBERG, 2010; LAPSINA et al., 2024). Although it aids in the categorization of neurological diseases according to the VITAMIN–D mnemonic (vascular, inflammatory, infectious, traumatic, toxic, anomalous, metabolic, idiopathic, neoplastic, and degenerative), it rarely establishes a definitive diagnosis (DEWEY & DA COSTA, 2016; DI TERLIZZI & PLATT, 2009; RASKIN & MEYER, 2016).

Although the association between cerebrospinal fluid abnormalities and neurological diseases has been extensively described in veterinary neurology textbooks and previous studies, comparative analyses of CSF findings across etiological groups remain limited, particularly in naturally occurring canine diseases from South American populations. Therefore, studies evaluating the distribution of CSF abnormalities according to disease etiology provide valuable epidemiological information and contribute to improving the interpretation of CSF analysis under

routine clinical conditions.

In this context, the present retrospective study characterized the CSF findings across etiological groups of canine neurological diseases based on physical, chemical, and cytological analyses. In addition to improving CSF interpretation, this study provided epidemiological data from a Brazilian referral population, complementing previous reports and supporting the interpretation of CSF findings in naturally occurring canine neurological diseases.

MATERIALS AND METHODS

Medical records of animals treated at the institution's veterinary hospital were retrospectively reviewed, and dogs that underwent CSF collection between January 1, 2018, and June 1, 2025, were identified. Dogs with a final clinical diagnosis of central nervous system disease and complete CSF analysis reports were included. Patients without a definitive diagnosis, with multiple diagnoses, or with incomplete reports were excluded.

The following data were collected: sex (male or female), body weight (kg), age (years), final clinical diagnosis, color (colorless, xanthochromic, or reddish), appearance (clear or turbid), total protein (TP; mg/dL), glucose (mg/dL), total nucleated cell count (TNCC; cells/ μ L), percentage of mononuclear cells (%MN), percentage of polymorphonuclear cells (%PN), and pleocytosis (absent, < 5 cells/ μ L; mild, 6–25 cells/ μ L; moderate, 26–100 cells/ μ L; or severe, > 100 cells/ μ L) (DI TERLIZZI & PLATT, 2009; LEVINE & COOK, 2020).

Final clinical diagnoses of central nervous system diseases were established based on the integration of clinical presentation, neurological examination, response to immunosuppressive therapy when applicable, positive SNAP® tests or PCR results, identification of infectious agents in CSF, diagnostic imaging (plain and contrast radiography, computed tomography, and magnetic resonance imaging), surgical findings, necropsy, and/or histopathology. Histopathology was considered the definitive diagnostic method whenever available. Dogs and their respective CSF samples were allocated into etiological groups according to the VITAMIN–D mnemonic (vascular, idiopathic, traumatic, toxic, anomalous, metabolic, inflammatory, infectious, neoplastic, and degenerative).

Categorical variables (sex, color, appearance, and pleocytosis) were expressed as frequencies, whereas continuous variables (age, body weight, TP, glucose, TNCC, %MN, and %PN) were summarized as median and interquartile range (Q1–Q3). Subsequently, the

data were subjected to factorial analysis of mixed data (FAMD), multinomial logistic regression, and Random Forest analysis using R software (version 4.2.3), with a significance level of 5%.

RESULTS

A total of 363 records of dogs that underwent CSF collection were identified during the study period. Of these, 276 patients were excluded, including 219 due to lack of a definitive diagnosis, four due to multiple diagnoses, and 53 due to incomplete CSF reports. After applying the inclusion criteria, 87 dogs were distributed into etiological groups according to the VITAMIN–D mnemonic. Of these, 75 were assigned to the inflammatory (10/75), infectious (21/75), neoplastic (10/75), and degenerative (34/75) groups, comprising the final study population. The remaining 12 dogs corresponded to etiological groups with low representation. Due to simultaneous CSF collection from CM and CL in 26/75 dogs, a total of 101 samples were obtained from the inflammatory (18/101), infectious (30/101), neoplastic (14/101),

and degenerative (39/101) groups.

The distribution of variables including sex, body weight, age, color, appearance, TP, glucose, TNCC, %MN, %PN, and pleocytosis across the four final etiological groups is presented in table 1. FAMD was used to visualize the dispersion of CSF samples according to the evaluated variables. No clustering of samples according to the inflammatory, infectious, neoplastic, and degenerative groups was observed, demonstrating considerable overlap in the multivariate distribution of CSF variables among the evaluated etiological groups.

Multinomial logistic regression revealed significant associations between specific variables and etiological groups, considering the degenerative group as the reference category. Increased body weight was associated with a lower likelihood of belonging to the inflammatory group (OR=0.802; $p=0.0017$). Increasing age was associated with a lower likelihood of belonging to the infectious group (OR = 0.705; $P = 0.0024$) and a higher likelihood of belonging to the neoplastic group (OR=1.576; $P = 0.0131$). Pigmented samples were associated with a lower likelihood of

Table 1 - Distribution of categorical and continuous variables of dogs (N = 75) and cerebrospinal fluid samples (N = 101), according to the inflammatory, infectious, neoplastic, and degenerative etiological groups.

-----Dog characteristics-----					
Variable		Inflammatory (n = 10)	Infectious (n = 21)	Neoplastic (n = 10)	Degenerative (n = 34)
Sex	Male	6	10	4	20
	Female	4	11	6	14
Age (years)*		6 (3–8)	3 (1–6)	10 (9–12)	8 (5–10)
Body weight (kg)*		5,4 (3.9–8.3)	8.5 (6.5–22.8)	18.2 (10.4–24)	10.5 (7.9–17.6)
-----CSF sample characteristics-----					
Variable		Inflammatory (n = 18)	Infectious (n = 30)	Neoplastic (n = 14)	Degenerative (n = 39)
Color	Colorless	11	29	12	26
	Xanthochromic	2	1	2	10
	Reddish	5	0	0	3
Appearance	Clear	13	23	13	35
	Turbid	5	7	1	4
Pleocytosis	Absent	8	11	10	28
	Mild	5	13	2	4
	Moderate	4	2	1	7
	Severe	1	4	1	0
Total protein (mg/dL)*		94 (37–138)	110 (50–216)	54 (45–123)	60 (33–120)
Glucose (mg/dL)*		71 (62–76)	68 (59–81)	70 (62–79)	75 (66–86)
TNCC (cells/ μ L)*		7.2 (1.1–37.2)	8.5 (2.2–18.7)	0.6 (0–5.2)	3,3 (1.1–7.7)
MN (% cells/ μ L)*		89 (2–100)	85 (62–98)	30 (0–90)	70 (0–100)
PN (% cells/ μ L)*		0 (0–25)	8 (0–30)	0 (0–0)	0 (0–42)

*Continuous variables are expressed as median and interquartile range (Q1–Q3).

Abbreviations: kg, kilograms; CSF, cerebrospinal fluid; mg/dL, milligrams per deciliter; μ L, microliter; TNCC, total nucleated cell count; MN, mononuclear cells; PN, polymorphonuclear cells; %, percentage.

belonging to the infectious (OR = 0.002; P = 0.0003) and neoplastic (OR = 0.048; P = 0.0319) groups. Increased glucose concentration was associated with a lower likelihood of belonging to the inflammatory group (OR = 0.913; P = 0.0022). An increase in %PN was associated with a lower likelihood of belonging to the infectious group (OR = 0.966; P = 0.0434). The presence of pleocytosis was strongly associated with a higher likelihood of belonging to the infectious group (OR = 22.403; P = 0.0053).

Although the Random Forest model achieved only moderate classification accuracy (60.4%), its results reinforce the multifactorial nature of CSF interpretation and the overlap among etiological groups. Sensitivity was highest for the degenerative group (74.36%), followed by the infectious (66.67%), inflammatory (38.89%), and neoplastic (35.71%) groups. Regarding variable importance, age showed the greatest contribution to classification (28.24%), followed by body weight (20.43%) and CSF color (16.50%). The remaining variables showed progressively lower contributions, including glucose (10.45%), %MN (8.80%), pleocytosis (6.53%), %PN (6.11%), sex (6.05%), TNCC (5.80%), TP (5.30%), and CSF appearance (1.58%).

The moderate classification performance obtained with the Random Forest model highlights that CSF analysis should not be interpreted as an isolated diagnostic tool. Instead, its greatest clinical value lies in its integration with neurological examination, diagnostic imaging, and complementary laboratory tests, reinforcing its role as an important component of the diagnostic investigation rather than a standalone method.

DISCUSSION

This retrospective study evaluated 101 CSF samples from 75 dogs, establishing useful criteria for the characterization of inflammatory, infectious, neoplastic, and degenerative neurological diseases based on the physical, chemical, and cytological parameters of CSF, as well as intrinsic patient characteristics.

The present study provided a retrospective evaluation of CSF findings across etiological groups of naturally occurring neurological diseases in dogs from a Brazilian referral population. Although many CSF abnormalities have been individually described in previous studies, comparative analyses across etiological groups remain limited. Therefore, these results complement the available literature by providing epidemiological data obtained under

routine clinical conditions and reinforce the clinical applicability of CSF analysis.

Inflammatory neurological diseases most commonly diagnosed in dogs correspond to meningoencephalitides of unknown origin (MUO) (BACH et al., 2023; DEWEY & DA COSTA, 2016), with an estimated prevalence ranging from 5–25% of central nervous system disorders (DIOP et al., 2026). The relatively lower glucose concentration in CSF observed in inflammatory diseases may be associated with alterations in transport across the blood–brain barrier (BBB) and increased metabolic consumption by glycolytic cells, such as neutrophils, lymphocytes, and monocytes (BAUD et al., 2017; RASKIN & MEYER, 2016).

Infectious neurological diseases occur predominantly in young and middle-aged dogs (DEWEY & DA COSTA, 2016), in agreement with the findings of the present study. Viral meningoencephalitides, frequently associated with canine distemper virus, represent the main infectious etiology in this species (BACH et al., 2023; DEWEY & DA COSTA, 2016). The higher prevalence in young dogs is related to immune system immaturity, regional circulation of the pathogen, high transmissibility, low vaccination coverage, and the large population of free-roaming dogs (DAY et al., 2020; SARCAHI et al., 2022).

The predominance of colorless CSF samples in the infectious group suggests a low likelihood of iatrogenic blood contamination or chronic pathological hemorrhage (DI TERLIZZI & PLATT, 2009; LEVINE & COOK, 2020; NGHIE & SCHATZBERG, 2010). In viral meningoencephalitis, pleocytosis with a lymphocytic pattern is frequently observed (BACH et al., 2023; DI TERLIZZI & PLATT, 2009; LEVINE & COOK, 2020; NGHIE & SCHATZBERG, 2010). In this context, increased %PN, commonly associated with neutrophilic or eosinophilic patterns, showed a lower likelihood of belonging to the infectious group (BACH et al., 2023; DI TERLIZZI & PLATT, 2009; LEVINE & COOK, 2020).

Neoplastic neurological diseases occur predominantly in older dogs (DEWEY & DA COSTA, 2016; MILLER et al., 2019). Dogs frequently develop spontaneous tumors, with meningioma and glioma being the most prevalent (MILLER et al., 2019; RISSI et al., 2024). Although the literature occasionally reports xanthochromia in CSF associated with necrotic or erosive tumors (DEWEY & DA COSTA, 2016; LOWRIE & ANDERSON, 2011; RASKIN & MEYER, 2016), the predominance of colorless samples in the neoplastic group suggested that the evaluated tumors exhibited an expansive or compressive pattern without

significant necrosis or erosion.

Degenerative neurological diseases are frequently observed in middle-aged dogs due to their chronic and progressive course (DEWEY & DA COSTA, 2016; SRUGO et al., 2011). Among these, intervertebral disc disease (IVDD) is a common cause of acute spinal cord injury in dogs, particularly in chondrodystrophic breeds (OLBY et al., 2020; WEE & NIN, 2025). Previous studies have reported a higher prevalence of IVDD in medium-sized dogs, with overweight status as a predisposing factor (WEE & NIN, 2025).

CSF analysis in patients with IVDD is highly variable, depending on lesion location, chronicity, and severity (LEVINE & COOK, 2020). CSF samples may be normal or show mildly inflammatory characteristics (SRUGO et al., 2011). The findings suggested a predominance of pigmented samples. In this context, subarachnoid hemorrhages secondary to disc extrusions may result in xanthochromic CSF (DEWEY & DA COSTA, 2016; RASKIN & MEYER, 2016). In contrast, pleocytosis is not commonly observed in degenerative diseases (NGHIEM & SCHATZBERG, 2010).

Although caudal neurolocalization of lesions justifies puncture at the CL (LAMPE et al., 2020), simultaneous collection at both sites is recommended, when clinically feasible, in order to increase the diagnostic sensitivity of CSF analysis (LAMPE et al., 2020; SUÑOL et al., 2021). Iatrogenic blood contamination resulting from traumatic puncture may interfere with TNCC and TP evaluation (MACNEILL et al., 2018). The erythrocyte/ μL threshold associated with these changes, as well as proposed correction formulas, are inconsistent and imprecise (BRUNE et al., 2022; MACNEILL et al., 2018). Therefore, reddish CSF samples were included in the analysis.

Although the findings are consistent with the existing literature, the present study complements the available evidence by providing epidemiological and clinical data from a Brazilian referral population, an underrepresented clinical setting in studies evaluating CSF findings according to the etiological classification of neurological diseases using CSF analysis. Prospective multicenter studies involving different geographic regions will be important to validate the present findings and improve the generalizability of the proposed associations.

CONCLUSION

The integrated analysis of CSF findings revealed useful criteria for the characterization of

the main etiological groups within the VITAMIN-D mnemonic. Inflammatory neurological diseases were characterized by dogs with lower body weight and CSF samples with relatively lower glucose concentrations. Infectious neurological diseases were characterized by younger dogs, predominantly colorless CSF samples, and marked pleocytosis. Neoplastic neurological diseases were characterized by older dogs and predominantly colorless CSF samples. Degenerative neurological diseases were characterized by dogs with intermediate body weight and age, predominantly pigmented CSF samples, and absence of pleocytosis. Beyond confirming previously recognized CSF patterns, the present study provided epidemiological data from a Brazilian referral hospital population that complement the available literature and reinforce the diagnostic value of cerebrospinal fluid analysis in the investigation of naturally occurring neurological diseases in dogs.

DATA AVAILABILITY STATEMENT

The raw data analyzed in the present study are available from the corresponding author upon reasonable request, subject to applicable institutional and confidentiality requirements.

ACKNOWLEDGMENTS

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001.

DECLARATION OF CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

AUTHORS' CONTRIBUTIONS

ABR contributed to Conceptualization, Data curation, Data analysis, Funding receipt, Research, Methodology, Data and experimental validation, Data presentation design, and Writing of the original manuscript. VCM and GIG contributed to Data curation and Methodology. VNH and FBL contributed to Methodology. AM and AK contributed to Tool provision and Methodology. DVB contributed to Conceptualization, Funding receipt, Methodology, Project administration, Supervision, Data and experimental validation, Data presentation design, and Writing – review and editing.

DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence tools were used exclusively for reviewing and improving the language and quality of the manuscript. The authors carefully reviewed and validated the final content.

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